

Are There Other Persistent Organic Pollutants? A Challenge for Environmental Chemists[†]

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The past 5 years have seen some major successes in terms of global measurement and regulation of persistent, bioaccumulative, and toxic (PB&T) chemicals and persistent organic pollutants (POPs). The Stockholm Convention, a global agreement on POPs, came into force in 2004. There has been a major expansion of measurements and risk assessments of new chemical contaminants in the global environment, particularly brominated diphenyl ethers and perfluorinated alkyl acids. However, the list of chemicals measured represents only a small fraction of the approximately 30,000 chemicals widely used in commerce (>1 t/y). The vast majority of existing and new chemical substances in commerce are not monitored in environmental media. Assessment and screening of thousands of existing chemicals in commerce in the United States, Europe, and Canada have yielded lists of potentially persistent and bioaccumulative chemicals. Here we review recent screening and categorization studies of chemicals in commerce and address the question of whether there is now sufficient information to permit a broader array of chemicals to be determined in environmental matrices. For example, Environment Canada's recent categorization of the Domestic (existing) Substances list, using a wide array of quantitative structure activity relationships for PB&T characteristics, has identified about 5.5% of 11,317 substances as meeting P & B criteria. Using data from the Environment Canada categorization, we have listed, for discussion purposes, 30 chemicals with high predicted bioconcentration and low rate of biodegradation and 28 with long range atmospheric transport potential based on predicted atmospheric oxidation half-lives >2 days and log air–water partition coefficients ≥ 5 and ≤ 1 . These chemicals are a diverse group including halogenated organics, cyclic siloxanes, and substituted aromatics. Some of these chemicals and their transformation products may be candidates for future environmental monitoring. However, to improve these predictions data on emissions from end use are needed to refine environmental fate predictions, and analytical methods may need to be developed.

Introduction

Since the publication of Silent Spring in the 1960s (1), it has been known that highly chlorinated compounds will be

persistent in the environment. With the advent of the electron capture detector, organochlorine pesticides (OCPs) such as DDT, DDE, dieldrin, toxaphene, and commercial chloroorganic chemicals such as PCBs began to be detected globally in environmental samples. Beginning in the 1970s many OCPs were banned in North America, western Europe, and Japan (dieldrin, 1971; DDT, 1972) and/or use was restricted (PCBs). The 1970s also saw the passage of numerous legislative acts, such as in the Toxic Substances Control Act (TSCA) in the United States, which required screening of new chemicals to anticipate substances that could be of concern. Similar registration and screening legislation was introduced in Japan (Chemical Substances Control Law, 1973), Europe (European EC-Existing Substances legislation 1981), Canada (Domestic Substances List, 1986), and other countries. Existing chemicals in commerce were largely “grandfathered”; i.e., the requirement for information on structure, toxicity, and other data for use in risk assessments was mainly limited to new substances.

International action on these and related chlorinated organics, such as polychlorinated dioxins/furans (PCDD/Fs), culminated in the signing of the Stockholm Convention on persistent organic pollutants (POPs) in 2001 (2). This agreement, which came into force in 2004 (although not ratified by the United States), identified 12 chlorinated chemical groups (8 individual OCPs, HCB, PCBs, and PCDD/Fs) for global bans or reduced emissions. The Convention defines criteria for screening of new POPs in terms of persistence, bioaccumulation, potential for long-range transport, and toxicity (2). Also, in Article 3.3, the Parties to the Convention should take measures to prevent the introduction of new POPs into commerce.

National and international environmental monitoring programs have continued to measure POPs since the 1970s. The monitoring of other persistent, bioaccumulative, and toxic (PB&T) substances has slowly added to the list of chemicals routinely determined in environmental media largely following the “analog” approach. For example, widespread measurement of polybrominated diphenyl ethers (PBDEs) utilizes existing methodology for PCBs and related compounds. Similarly, chlorinated benzenes, chlorinated naphthalenes (PCNs), and chlorinated paraffins all can be isolated with the same methodology and quantified with similar instrumental techniques (3). However, the vast majority of the approximately 30,000 chemical substances in wide commercial use (>1 t/y) are not measured in environmental media, and their emissions and fate are unknown. If there are other, previously unidentified POPs, they are likely to be found in the list of chemicals in commerce or as degradation products of these substances. An example of the latter case is the discovery of the global distribution of PFOS, a highly persistent and bioaccumulative compound

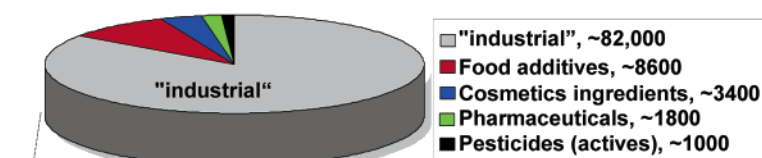
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A. Breakdown of the Chemicals in commerce – USA



B. "Industrial" Chemicals in commerce – US TSCA inventory

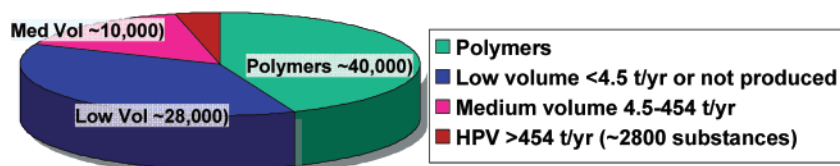


FIGURE 1. Estimated number and categories of chemicals in commerce registered for use in the United States over the past 30 years. Not all chemicals may be in current use. Similar proportions would be anticipated in other countries.

which is a degradation product of perfluorooctane sulfonamido-alcohols used in perfluoro polymers (4–6).

The extent to which humans and wildlife are exposed to the vast array of anthropogenic chemicals and their degradation products, along with related naturally occurring compounds, is an important issue (7) but is beyond the scope of this article. Here we focus on recent developments in screening and categorizing of chemicals in commerce for P&B characteristics. We have mainly considered P&B, and long range atmospheric transport (LRAT) characteristics, such as atmospheric oxidation half-life ($AO\ t_{1/2}$), because, as discussed by Mackay et al. (8), only intensive properties such as degradation half-lives and partition coefficients are meaningfully ranked because they are independent of quantity of substance. We have developed a list of chemicals, based on data from the recent screening of the Canadian Domestic (existing) Substances List (DSL), that meet the criteria for P, B, and LRAT characteristics as outlined in the Stockholm Convention. We address the question of whether there is sufficient confidence in this information to permit environmental analytical chemists to proceed to identify candidate chemicals in environmental matrices.

How Many Commercial Chemicals?

About 8,400,000 substances are commercially available and 240,000 are reported to be inventoried/regulated chemicals according to the CAS web site (9). The European Inventory of Existing Commercial Chemical Substances (EINECS) lists more than 100,000 substances that were marketed in Europe between 1971 and 1981 when the inventory was compiled (10). The U.S. EPA TSCA inventory consists of about 82,000 chemicals (Figure 1A) (11). Approximately 43% of the substances on the TSCA inventory are polymers that are thought to present less risk to the environment. TSCA does not cover nuclear material, firearms and ammunition, or substances used only as pesticides, food, food additives, pharmaceuticals, and cosmetics. Combined with pesticides, food additives, drugs and cosmetics, there are as many as 100,000 chemicals that have been registered for use in commerce in the United States over the past 30 years, and numbers are similar in the EU and Japan.

Production volume is a key indicator in the search for new P&B chemicals because most legacy POPs (except PCDD/Fs) were, at one time, high production volume chemicals (HPVCs). The Organization for Economic Cooperation and Development (OECD) lists 4800 chemicals with global production of >1000 tonnes/year (t/y) (12). The Inventory Update Rule (IUR) results in partial updating of the sub-

stances on TSCA by requiring reporting of chemicals manufactured or imported at >4.5 t/y. In the United States, the IUR for 2002 has approximately 9000 organic chemicals that are produced or imported at >4.5 t/y with approximately 2,800 produced in excess of 454 t/y (13). Another 30,000 are produced/imported in low volume (<4.5 t/y) and were not reported in the 2002 IUR. Some chemicals in this low volume group may no longer be in production. In Europe, 7800 chemicals are listed as low production volume (LPV; >10 t/y and <1000 t/y) (10) and the estimated number of substances marketed in volumes above 1 t/y is 30,000 (14). The available toxicity and exposure data for HPVCs were identified as inadequate for risk assessment in the mid-1990s (11). More recently, programs such as the U.S. EPA's HPVC Challenge (15), the OECD's HPVC program (12), and international chemical industry initiatives (16) are part of a coordinated effort to develop adequate screening information data sets (SIDS) for all HPVCs.

Figure 1A also shows the approximate numbers of current use pesticides (CUPs), pharmaceuticals, cosmetics ingredients, and food additives in U.S. commerce. Numbers in world commerce are expected to be similar. For the most part, these substances are regulated by other legislation, e.g., Food and Drug or Pesticides, rather than Existing Chemical legislation (17), however, they may be included on existing chemical lists, e.g., EINECS includes some older CUPs. A key difference between these substances and most of the "existing" industrial chemicals is that there are often very substantial datasets available on measured physical–chemical properties, degradation rates and products, and toxicity. In contrast, for the majority of industrial chemicals in commerce, only predicted properties are available.

In summary, the lists of "existing" industrial chemicals in commerce (Figure 1A & B) are more likely to contain previously unidentified PB&Ts. There are general criteria that need to be met to identify an organic chemical that may be of long-term concern as a P & B chemical.

- **Production Volume.** The chemical has to have a reasonable amount of production in order for it to be detected in environmental matrices, i.e., so that exposure can be assessed. As a guide to how much production, Webster et al. (18) noted that 3 kt of a volatile substance evenly distributed in the lower troposphere represents a concentration of 1 ng/m³, an amount readily detectable by high-volume and passive air sampling.

- **Use Profile.** The chemical has to be used in a way that it can be released to the environment. Mode of entry information is critical to exposure assessment (18). This is

TABLE 1. Screening Criteria for Identifying Chemicals that are PB&T and Potential POPs

organization	long-range transport			persistence $t_{1/2}$ (d)			bioaccumulation		toxicity
	remote measurement	VP ^a (Pa)	AO ^b $t_{1/2}$ (d)	water	soil	sediment	BAF/ BCF	Log K_{ow}	
UNEP (2)	yes	or <1000	2	>60	>180	>180	5000	5	risk profile
UNECE (25)	yes	or <1000	2	>60	>180	>180	5000	5	risk profile
Canada (26)	yes			>180	>180	>360	5000	5	CEPA defined
US EPA TSCA PBT ban (27)				>180			5000		toxicity data
US EPA TSCA release controls (27)				>60			1000		toxicity data
OSPAR (28)				NIB ^c			500	4	NOEC <0.1 mg/L
REACH Annex XII and EU Technical Guidance Document (29) - PBTs				>40 (fresh)		120 (fresh)	2000		chronic NOEC <0.01 mg/L or CMR ^d or EDC
REACH Annex XII and EU Technical Guidance Document (29) - vPvBs				>60 (marine)		180 (marine)			not applicable
				>60		>180	5000		

^a Vapor pressure (Pa). ^b Atmospheric oxidation half-life (days). ^c Not inherently biodegradable. ^d CMR = carcinogenic, mutagenic, or toxic for reproduction category; EDC = endocrine disrupting.

often difficult to anticipate, e.g., PBDE additives in plastics and perfluoroalkyl alcohol residuals in fluorinated polymers were not initially thought to be a problem.

• **Physical–Chemical Characteristics.** The chemical has to have some chemical features to make it resistant to degradation and more likely to bioaccumulate (e.g., halogenated, highly branched, multiple rings, acyclic) and, as well, the parent compound or degradation product must be capable of being transported long distances atmospherically or via ocean currents.

Screening of Existing Chemical Lists for PB&T and POP Characteristics

Since 1977 the Interagency Testing Committee (ITC) (19), which reports to the Administrator of the U.S. EPA, has screened ~40,000 TSCA substances and recommended ~3000 for further toxicity testing (20, 21). Reports by the ITC (e.g., ref 22.) and listings on ITC's Priority Testing List (19) are a potentially good source of chemicals of environmental concern although they do not include physical–chemical properties, production volume, or use information. As software for Quantitative Structure Property Relationships (QSPRs) has improved over the past 10–15 years, it has become possible to screen large lists of chemicals in commerce (discrete substances, i.e., not uncharacterized mixtures or polymers) for P&B and POPs criteria as defined in Table 1 (20, 21, 23). Quite similar criteria have been adopted by UN and national programs. Rodan et al. (24) in reviewing the UNEP/UNECE criteria noted that they “.. tend to isolate a limited number of clearly hazardous POPs from the majority of organic chemicals, while not being so stringent that the ability to respond to as yet unidentified risks is seriously compromised”. Recently the use of overall persistence (P_{ov}), which accounts for both degradation half-lives in individual media and environmental partitioning has been proposed as a more robust approach to evaluating chemicals rather than single media half-lives (30). However, given the wide use of single media half-lives for screening chemicals we have not calculated or used P_{ov} values in this overview.

Walker and Carlsen (23) examined 8511 chemicals, with 1998 TSCA IUR production volumes (>4.5 t/y), to screen for persistence and bioaccumulation potential. This screening used U.S. EPA's “PBT Profiler” which uses a Level III fugacity mass balance model to predict persistence (31), and the Degradation Effects Bioconcentration Information Testing Strategies (DEBITS), both of which rely on the BIOWIN QSPR programs (EPISuite (32)) for predicting persistence. The

bioaccumulation potential was predicted by the BCFWIN program in EPISuite. Bioconcentration factor (BCF) and probability of biodegradation (BDP) were predicted yielding 56 chemicals with medium bioaccumulation (BCFs >1000) and persistence (BDPs < 2). This screening identified 10 highly persistent (sediment half-life = 1620 days) and moderately bioaccumulative chemicals (BCF >1000 and <5000). Interestingly, three were perfluorinated while seven others were non-halogenated but with multiple aromatic and/or aliphatic rings. Earlier screening of about 1000 chemicals on TSCA by Clements et al. (33) for persistence and bioaccumulation had identified 80 compounds with log K_{ow} 4.3–8.0 and persistence >30 days, of which 34 were HPVCs (>454 t/y). The chemicals identified by Walker and Carlsen (23) and Clements et al. (33) are listed in Supporting Information Table S1.

Possibly the most extensive screening and categorization of existing industrial chemicals has taken place between 2000 and 2006 in Canada under the Canadian Environmental Protection Act (CEPA) (see Supporting Information for additional details). An update of CEPA in 1999 required that Canada's DSL be categorized for PB&T characteristics. This applies to existing chemicals manufactured or imported into Canada at >100 kg in 1986 (34). Thus the production volume threshold is 10-fold lower than for most other existing substances lists, however, it is based on mid-1980s data. About half of the 23,000 substances on the DSL (11, 713) were assigned log K_{ow} values (16% were measured values). The other half were of “unknown or variable composition and biologicals” (UVCBs), or were polymers, metals and inorganics, organo-metallics, or organometal salts and could not be assigned physical properties using QSPRs. About 21% (2320) of the 11,317 individual organic chemicals had predicted log K_{ow} ≥ 5, a common screening criterion for bioaccumulation potential (Table 1). Predicted BCFs using the BCFWIN model (32) for 3.2% of the 11,317 compounds were >5,000 (Figure 2) and 16% had predicted biodegradation half-lives of >180 days.

Other projects have examined large lists of chemicals for persistence and toxicity. Öberg (35) applied QSPRs for baseline toxicity to fish (acute toxicity to fathead minnows), and for atmospheric oxidation by hydroxyl (OH) radical reaction, to 98,000 compounds on the SMILESCAS Database (SRC, North Syracuse, NY). Applying the two QSPRs sequentially, 50,074 compounds were judged to be within the domain of applicability for both models. In all, 1653 compounds were predicted to meet criteria of persistence (AO $t_{1/2}$ >2 days)

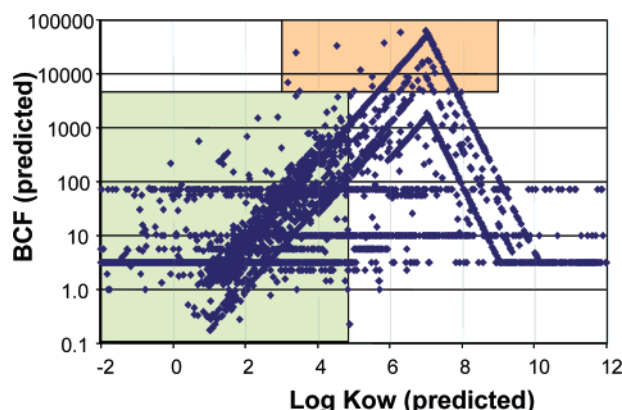


FIGURE 2. Log K_{ow} and BCF of 11,317 substances on the Canadian DSL using the BCFWIN model (BCF – wet weight basis). The data points consist of both empirical (measured) and predicted data. The predicted data tend to cluster on the line due to the BCFWIN algorithms. About 21% have log $K_{ow} > 5$ and 3.2% have BCF > 5000 (highlighted areas).

and toxicity (fish acute toxicity $LC_{50} < 10$ mg/L) and 88% of these were halogenated. As expected, halogenation was associated with the highest toxicity and persistence. Wiandt and Poremski (28) describe the results of a ranking and prioritization of substances for PB&T characteristics by the Oslo-Paris Commission (OSPAR) for impacts on the marine environment. The initial selection involved examining the Nordic Substance Database (about 18,000 substances), the Danish Miljøstyrelsen QSPR database (more than 166,000 substances) and the database of The Netherlands' BKH/Haskoning report (about 180,000 substances) against PB&T criteria (Table 1). This was narrowed down to 400 substances, of which only 203 could be ranked because production volumes and use characteristics were not available for most chemicals. Ultimately 12 compounds (Supporting Information Table S1) were identified for priority action by OSPAR (36). Lerche et al. (37) drew upon some of the same large chemical databases as Öberg (35) and Wiandt and Poremski (28), to identify compounds with LRAT potential, as well as P&B characteristics. They identified 42 chemicals with P & B characteristics and 12 compounds, all halogenated, which were predicted to meet all POP screening criteria (Supporting Information Table S1). Several of the compounds in their top 12 (dicofol, PCNs, and hexachlorobutadiene) are now being considered for the United Nations Economic Commission for Europe (UNECE) POPs list (38).

These screening programs discussed above have already resulted in the development of a much broader array of information on structure and physical–chemical properties of existing chemicals in the past 5 years than was available previously. However, there are many limitations inherent in the process. The available QSPRs typically have training sets of <1000 substances. For example, BCFWIN (32) and the BCF Max model (39) estimate BCFs based on the dataset of Meylan et al. (40) of 694 chemicals, of which 610 are non-ionic. The exception is the QSPR for log K_{ow} , KOWWIN, which has 13,000 experimental K_{ow} values. Simplified Molecular Input Line Entry System (SMILES) notations are usually used for model inputs and make possible rapid batch analysis of thousands of compounds. However, lack of structural information for some substances, especially those that are UVCBs, results in many substances being omitted from the QSPR screening (23, 37). The study by Öberg (35) illustrated the broad applicability of QSPRs as well as their limitations. About 50% of the chemicals were judged to not be within the zone of applicability of the QSPRs even though structural information was available. When compared to the criteria in Table 1, the possibility of false negatives is a concern for

regulators while false positives are a concern from a chemical manufacturer's perspective.

Upcoming changes to chemical regulation and assessment are likely to improve the amount of information available on uses and properties of existing substances. Under the REACH regulation, which is expected to be adopted by early 2007 in the European Union, registration of substances manufactured or imported in volumes starting at 1 t/y will be required as well as risk assessments of existing substances marketed in volumes at or above 10 t/y (41). In 2006, the U.S. EPA's IUR will include consumer end uses of chemicals for substances produced or imported at > 136 t/y although the threshold for reporting will be raised to 11.4 t/y (13).

LRAT Characteristics to Distinguish POPs

Evidence for LRAT is part of the UNEP, UNECE, and Canadian criteria but not TSCA or REACH (Table 1). Although there is much overlap, this characteristic distinguishes atmospherically transported substances from other P&B chemicals that may have local or regional dispersion mainly via water, water-borne particles, or sewage sludge. Fenner et al. (42) compared the results of multimedia LRAT models. Two global scale models, ChemRange and GloboPOP, identify chemicals with log air–water partition coefficients (log K_{aw}) ≥ 5 and ≤ 1 as having high LRAT potential. Compounds with log octanol–air partition coefficient (K_{oa}) > 13 are predicted to undergo LRAT as aerosol-sorbed chemicals in these models. Both assume no degradation for evaluative purposes. Overall persistence were highly correlated among all multi-media models (42), as was LRAT potential, and differences were largely determined by the chemical properties. Application of these models to the vast array of existing chemicals is technically feasible and, indeed, screening has been performed routinely (43) using models for Characteristic Travel Distance (44) and Effective Travel Distance (45). However, the high uncertainties of some key physical properties such as log K_{oa} and degradation rates, for existing chemicals, affect the application of large multicompartiment LRAT models as they do for the prediction of persistence.

Potential P&B and LRAT Substances

Presented here for discussion purposes are two lists of chemicals with P&B and LRAT characteristics based on data assembled for the Canadian DSL categorization (See Supporting Information and ref 34). Table 2 lists 30 chemicals sorted by highest predicted BCF and then by degradation half-life extrapolated from BIOWIN (34), while Table 3 lists chemicals sorted by key LRAT parameters, AO $t^{1/2}$ and log K_{aw} . Those in Table 2 were all in use or manufactured at > 1 t/y in the 1980s in Canada and 23 of 30 are on current U.S. or European lists with production generally > 10 t/y. Seven are, or were, HPVCs when last surveyed, appearing on OECD (12) and/or the U.S. EPA lists (15). They are a diverse group: 9 of 30 are halogenated, 2 are substituted organophosphates, 1 is a cyclic siloxane, and the remainder are mainly substituted aromatics. The predicted BCFs for the two QSPR models BCFWIN (32) and BCFmax (39) were highly correlated. However, they differ below log BCF of 4.5, with values estimated by BCFWIN up to 1 order of magnitude lower, illustrating that compounds can be classified differently (i.e., exceeding the log BCF = 3.7 (or 5000) threshold under the UNECE, UNEP, and Canadian screening criteria (Table 1)) depending on the QSPR. The environmental media in which the compounds are predicted to accumulate are also diverse with 1 in air, 2 in air and soil, 17 in soil, 6 in water, and 4 in soil and water. All are predicted to be very persistent in soil and water (all biodegradation $t^{1/2}$ values > 60 d; most > 182 d).

Table 3 lists the top 30 compounds in the Canadian DSL sorted by key LRAT parameters AO $t^{1/2}$ and log K_{aw} . For all

TABLE 2. Top 30 Bioaccumulative and Persistent Substances Based on Data Assembled for the Environment Canada DSL Categorization^a

no.	chemical name	CAS no.	log K_{ow}	Log BCF ^b	log BCF ^c	degradation ^d $t_{1/2}$ (d)	media ^e	production volume ^f
1	[1,1'-biphenyl]-4,4'-diamine, <i>N,N'</i> -bis(2,4-dinitrophenyl)-3,3'-dimethoxy-	29398967	6.94	4.74	4.65	182	W	LPVC
2	benzenamine, 4,4'-[(1-methylethylidene)bis(4,1-phenyleneoxy)]bis-	13080869	6.88	4.76	4.60	182	S	TSCA
3	1-naphthalenemethanol, α,α -bis[4-(dimethylamino)phenyl]-4-(phenylamino)-	6786830	7.21	4.63	4.52	182	W	LPVC
4	1-octanesulfonamide, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptafluoro- <i>N</i> -(2-hydroxyethyl)- <i>N</i> -methyl-	24448097	7.29	4.59	4.42	182	A	HPV
5	spiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one, 3',6'-bis(diethylamino)-	509342	6.63	4.82	4.41	182	S	LPVC
6	spiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one, 6-(diethylamino)-3-methyl-2-(phenylamino)-	29512490	7.32	4.57	4.38	182	S	HPV
7	peroxide, [1,3(or 1,4)-phenylenebis(1-methylethylidene)]bis[(1,1-dimethylethyl)]	25155253	7.34	4.56	4.35	182	S	HPV
8	peroxide, (1,1,4,4-tetramethyl-1,4-butanediyl)bis[(1,1-dimethylethyl)]	78637	6.55	4.82	4.35	182	AS	HPV
9	anthra[2,1,9-def:6,5,10-d'e'f']diisoquinoline-1,3,8,10(2H,9H)-tetrone, 2,9-bis(3,5-dimethylphenyl)-	4948156	7.36	4.54	4.31	182	W	LPVC
10	anthra[2,1,9-def:6,5,10-d'e'f']diisoquinoline-1,3,8,10(2H,9H)-tetrone, 2,9-bis(4-chlorophenyl)-	2379773	6.46	4.83	4.28	182	W	LPVC
11	spiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one, 2',4',5',7'-tetrabromo-3',6'-dihydroxy-	15086949	6.91	4.75	4.22	182	S	LPVC
12	1,4-benzenediamine, <i>N,N</i> -di-2-naphthalenyl-	93469	6.39	4.83	4.22	60	W	LPVC
13	cyclohexasiloxane, dodecamethyl- (D6)	540976	6.33	4.83	4.17	60	A	LPVC
14	perylene[3,4-cd:9,10-c'd']dipyran-1,3,8,10-tetrone	128698	6.26	4.82	4.12	182	S	LPVC
15	1-naphthalenepropanol, α -ethenyldecahydro-2-hydroxy- α ,2,5,5,8a-pentamethyl-, [1R-[1 α (R*),2,4a,8a α]]-	515037	6.00	4.78	3.92	182	S	
16	benzene, 1,1'-oxybis-, pentabromo deriv. (pentaBDE)	32534819	7.66	4.35	3.91	182	S	HPV
17	adenosine, <i>N</i> -benzoyl-5'-o-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-	64325786	5.94	4.76	3.88	182	WS	
18	methylum, bis(4-amino-3,5-dimethylphenyl)(2,6-dichlorophenyl)-, phosphate (1:1)	72812396	5.94	4.76	3.88	182	WS	
19	ethanol, 2,2'-[(1-methylethylidene)bis[(2,6-dibromo-4,1-phenyleneoxy)]bis-	4162452	6.78	4.79	3.87	182	S	LPVC
20	benzenamine, 4,4',4''-methylidynetris[<i>N,N</i> -dimethyl-	603485	5.90	4.75	3.84	182	WS	TSCA
21	peroxide, (1,1,4,4-tetramethyl-2-butyne-1,4-diyl)bis[(1,1-dimethylethyl)]	1068275	5.84	4.73	3.80	182	AS	TSCA
22	cyclododecane, 1,2,5,6,9,10-hexabromo- (HBCD)	3194556	7.74	4.29	3.79	60	S	HPV
23	benzene, 1,1'-(chlorophenylmethylene)bis[4-methoxy-	40615369	5.74	4.69	3.72	60	S	
24	1,3-isobenzofurandione, 4,5,6,7-tetrabromo-	632791	5.63	4.64	3.63	182	S	LPVC
25	propanedinitrile, [[4-[[2-(4-cyclohexylphenoxy)ethyl]ethylamino]-2-methylphenyl]methylene]-	54079537	7.88	4.18	3.60	182	WS	LPVC
26	phosphonium, triphenyl(phenylmethyl)-, salt with 4,4'-[2,2,2-trifluoro-1-(trifluoromethyl)ethylidene]bis[phenol] (1:1)	75768659	5.54	4.59	3.56	182	S	
27	5H-3,5a-epoxynaphth[2,1-c]oxepin, dodecahydro-3,8,8,11a-tetramethyl-	57345194	5.47	4.55	3.51	182	S	
28	oxirane, 2,2',2''-[1,2-ethanediyliidenetetrakis(4,1-phenyleneoxy)methylene]]tetrakis-	7328974	5.46	4.55	3.50	182	S	HPV
29	phosphorous acid, (1-methylethylidene)di-4,1-phenylene tetrakis[(3-ethyl-3-oxetanyl)methyl] ester	53184751	7.96	4.12	3.49	182	S	LPVC
30	1H-indene, 2,3-dihydro-1,1,3,3,5-pentamethyl-4,6-dinitro-	116665	5.39	4.51	3.45	182	S	

^a Chemicals were sorted by (a) BCF calculated with the BCF Max and BCFwin models and (b) biodegradation $t_{1/2}$ Life. Only substances also listed on either TSCA and/or EINECS lists of chemicals in commerce were included. ^bBCF max estimate by the model of Dimitrov et al. (39). ^c BCF values created by BCFWIN v 2.15. ^d Ultimate degradation $t_{1/2}$ (day) using Ultimate Survey Model in SRC's BIOWIN model, v 4.01 which predicts mineralization. Results from this model have been converted to half-lives based on an extrapolation procedure outlined in the Environment Canada DSL categorization guidance document (34). ^e The environmental distribution estimated using a level 1 fugacity model. A = air, S = soil, W = water. ^f All substances reported to be used at > 1 t/y in Canada in the 1980s. HPV = Substance is listed on OECD HPV chemical list (12) and/or U.S. EPA HPV list (15); LPVC = substance produced or imported in the EU at > 10 t/y (10); TSCA = produced or imported in the U.S.A at > 4.5 t/y

11,317 substances, 37% were found to have predicted log K_{aw} ≥ 5 and ≤ 1 which would indicate high LRAT potential if persistent in the atmosphere. However, of the 1200 compounds with log K_{aw} ≥ 5 and ≤ 1 and predicted BCF > 5000 only 28 compounds had (predicted) AO $t_{1/2}$ > 2 d. This group includes far more halogenated compounds (24/30) than the list in Table 2 reflecting the stability of the halogen-carbon bond to OH-radical reactions. There are also more substituted single aromatic ring compounds reflecting the selection of compounds with log K_{aw} ≥ 5 . While all are listed on the

Canadian DSL and EINECS only 5 are HPVcs and 13 of 30 have production > 4.5–10 t/y. Thus it is possible that the remaining 17 are not in current production or are produced in amounts much smaller than 10 t/y in Europe or the United States.

Still a Need for Scientific Judgment

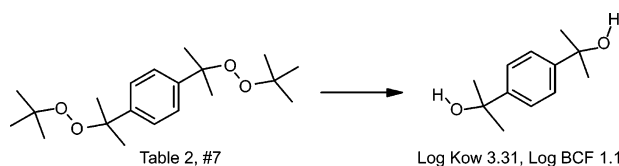
The QSPRs and data used to select the chemicals in Tables 2 and 3 allow for screening of thousands of chemicals and the identification of chemicals of high concern. However,

TABLE 3. Top 30 Persistent and Bioaccumulative Substances with long Range Atmospheric Transport Potential Based on Data Assembled for the Environment Canada DSL Categorization

no.	chemical name	CAS no.	degradation ^b $t_{1/2}$ (d)	AO ^c $t_{1/2}$ (d)	Log BCF ^d	log K_{aw} ^e	production volume ^f
1	1,3-isobenzofurandione, 4,5,6,7-tetrachloro-	117088	182	338.4	3.9	-4.1	HPV
2	benzenethiol, pentachloro-	133493	182	76.7	4.7	-2.3	HPV
3	benzene, 1,1-oxybis-, hexabromo deriv. (hexaBDE)	36483600	182	30.4	3.6	-4.7	TSCA
4	1,3-cyclopentadiene, 1,2,3,4,5,5-hexachloro- (HCCP)	77474	182	27.2	3.9	-1.1	HPV
5	benzene, 1,3,5-tribromo-	626391	60	22.0	3.9	-1.9	LPVC
6	benzene, 1,1-oxybis-, pentabromo deriv. (pentaBDE)	32534819	182	19.4	4.4	-4.3	HPV
7	cyclohexane, tribromotrichloro-	30554735	60	16.9	3.8	-3.4	
8	cyclohexane, tetrabromodichloro-	30554724	60	16.4	3.9	-3.9	
9	cyclohexane, 1,2,3,4,5-pentabromo-6-chloro-	87843	60	15.7	4.0	-4.4	TSCA
10	benzene, 1,3-diiodo-	626006	37.5	12.6	3.6	-1.9	
11	sulfonium, triphenyl-, chloride	4270706	37.5	8.6	4.6	-4.2	
12	benzene, 1-(1,1-dimethylethyl)-3,4,5-trimethyl-2,6-dinitro-	145391	60	7.3	4.4	-4.9	
13	benzene, 1,3,5-tribromo-2-methoxy-4-methyl-	41424366	60	7.2	4.4	-3.0	
14	benzene, 1,1-oxybis-, tetrabromo deriv.	40088479	182	7.1	4.8	-3.9	
15	peroxide, bis(2,4-dichlorobenzoyl)	133142	182	6.1	4.8	-4.4	TSCA
16	benzene, 1,2,3,4-tetrachloro-5,6-dimethoxy-	944616	182	4.4	4.1	-3.6	
17	peroxide, bis(4-chlorobenzoyl)	94177	60	4.3	4.0	-4.1	
18	butanoic acid, 3,3-bis[(1,1-dimethylethyl)dioxy]-, ethyl ester	55794202	60	3.4	4.2	-4.1	TSCA
19	1,1-biphenyl, 4-bromo-	92660	37.5	3.1	3.9	-2.2	
20	silane, dichlorodiphenyl-	80104	37.5	2.7	4.3	-2.5	HPV
21	benzene, 1-chloro-2-[2,2-dichloro-1-(4-chlorophenyl)ethyl]-	53190	182	2.5	4.7	-2.8	
22	naphthalene, dichloro-	28699889	37.5	2.4	3.8	-1.9	
23	cyclotetrasiloxane, 2,2,4,6,6,8-hexamethyl-4,8-diphenyl-, <i>cis</i> -	33204761	37.5	2.2	4.4	-1.9	
24	cyclohexane, 1,2-dibromo-4-(1,2-dibromoethyl)-	3322938	37.5	2.2	4.4	-2.8	TSCA
25	cyclododecane, 1,2,5,6,9,10-hexabromo- (HBCD)	3194556	60	2.1	4.3	-4.2	HPV
26	benzenemethanol, α -(trichloromethyl)-, propanoate	31643148	60	2.0	3.66	-4.4	
27	pyridine, 4-(4-chloro-3-propylphenyl)-	73398875	60	2.0	4.02	-4.5	
28	butanoic acid, 3,3-bis[(1,1-dimethylpropyl)dioxy]-, ethyl ester	67567231	60	2.0	4.76	-3.8	TSCA
29	propanoic acid, 2-methyl-, 2,2,2-trichloro-1-phenylethyl ester	72929023	60	1.9	4.04	-4.2	
30	cyclopropa[d]naphthalen-3(1H)-one, octahydro-2,4a,8,8-tetramethyl-, [1aS-(1 α ,2 α ,4 α ,8 α R*)]-	25966794	60	1.7	3.80	-2.3	

^a Substances were sorted by atmospheric oxidation $t_{1/2}$ (>2 day) and air-water partition coefficient ($\log K_{aw} \geq 5$ and ≤ 1). Only substances also listed on either TSCA and/or EINECS lists of chemicals in commerce were included. ^b Ultimate degradation $t_{1/2}$ (day) using Ultimate Survey Model in SRC's BIOWIN model, v 4.01. Results from this model have been converted to half-lives based on an extrapolation procedure outlines in the categorization guidance document (34). ^c Atmospheric oxidation half-life from the hydroxyl radical reaction half-lives predicted by SRC's AOPWIN program, v 1.91. The AOPWIN does not make any adjustment for chemicals that are not in the vapor phase (adsorbed to particulate matter), which for some chemicals with low vapor pressures or K_{oa} values could be quite important; it is generally believed that particulate sorbed chemicals are not reactive. ^d BCF max model of Dimitrov et al. (39). ^e Log air-water partition coefficient calculated from Henry's law constant (298 K). ^f All substances reported to be used at >0.1 t/y in Canada in the 1980s. HPV = Substance is listed on OECD HPV chemical list (12) and/or U.S. EPA HPV list (15); LPVC = substance produced or imported in the EU at >10 t/y (10); TSCA = produced or imported in the U.S.A at >4.5 t/y.

for a variety of reasons, some of these chemicals on further evaluation are not of concern as P&B chemicals. For example, the peroxides in Table 2 (nos. 7 and 8) are HPV chemicals, used as cross linking agents for rubber, and the peroxide would be degraded during processing. Thus, the chemical that needs to be assessed is the dialcohol product and this has a much lower K_{ow} and BCF and therefore, would not be a P&B substance.

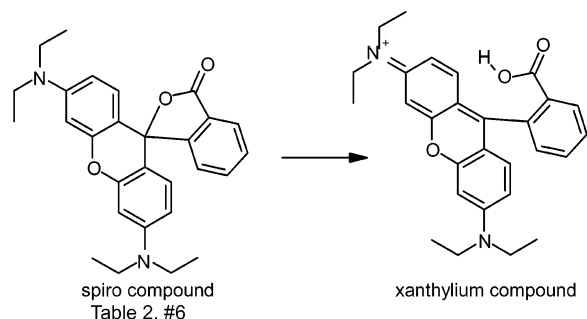


Another example of a chemical that is very reactive and will be degraded in the environment is oxirane, 2,2,2,2-[1,2-ethanediyliidenetetrakis(4,1-phenylene-oxymethylene)]tetrakis (no. 28 Table 2) which has four epoxide groups. One might expect that such a reactive chemical should not get a high persistence rating from the QSPR programs, but QSPRs are not infallible; thus the need for expert judgment. For this chemical, the chemical hydrolysis program in EPISuite (32) only estimates the second-order acid-catalyzed rate ($t_{1/2}$ = 62 years) and not the neutral hydrolysis rate (a warning is given). Even if the neutral chemical hydrolysis rate was

available, it is not used for the persistence calculation; only the BIOWIN ultimate survey model is used presently. The BIOWIN program recognizes the epoxides as aliphatic ethers (which they are, but highly strained) which are considered to be functional groups which lead to more persistence. In this case, instead of being a catalyst for cross linking like the peroxides, these epoxides (oxirane rings) react with other functional groups to cause cross linking; any residue compound in the polymer matrix might leach out but would not be stable in the environment. The hydrolysis product might be worth consideration but it would have a considerably lower $\log K_{ow}$ than the four epoxide compound (tetra glycol: $\log K_{ow}$ 1.22, $\log BCF$ -0.4).

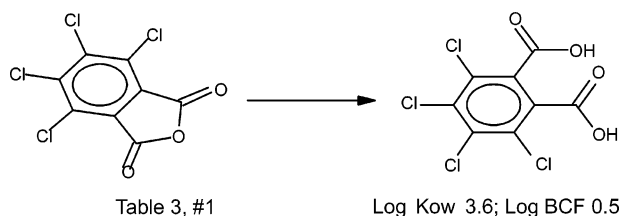
In contrast to the chemicals discussed above, there are some chemicals that are interesting as possible P&B candidates. For example, there are three spiro[isobenzofuran]s in Table 2. One (no. 6) is a TSCA HPV and during 1994 and 1998 had production volumes of 454–4540 t/y dropping to 227–454 t/y in the most recent reporting year (2002). However, it appears that these spiro compounds are used to synthesize xanthylum compounds (there are 5 xanthylum compounds on the DSL) and are synthetic intermediates. Synthetic intermediates are generally not good candidates because the chemicals are generally consumed during manufacture and not released to the environment. Thus, the chemical is converted to another chemical which should be

the target for PB&T assessment. However, there are some exceptions. For example, linear alkylbenzenes (LABs) are used to synthetically produce linear alkylbenzene sulfonates (LAS) surfactants, but a small amount of LABs remain in the LAS and LABs have been detected in the environment (46). Synthetic intermediates need to be carefully assessed for how much of the starting material remains as an impurity in the product and how likely the product is to be released to the environment.



Another example is tetrachlorophthalic anhydride (TCPA; Table 3 no. 1) a chemical intermediate and flame retardant in epoxy resin, plastics, paper, and textiles, which is predicted to have a long $AO\ t^{1/2}$. TCPA has been measured in occupational settings (47) but not, to our knowledge, in environmental media. As an anhydride, it may hydrolyze rapidly in water or on plant or soil surfaces and thus its probable degradation product, the dicarboxylate, may be a more appropriate target analyte. However, the $\log K_{ow}$ value will be much lower (3.63) and dependent upon the pH and the estimated $\log BCF$ value of 0.50 (BCFWIN ionic compounds) would not meet the BCF criteria. This may also be the case for tetrabromophthalic anhydride (Table 2, no. 24).

In general degradation products, formed by hydrolysis or



oxidation, are more polar and less bioaccumulative. On the other hand, the PFAs are examples of persistent and bioaccumulative degradation products, while phenolic oxidation products of halogenated aromatics, such as hydroxy-PCBs, may be bioaccumulative and toxic (48).

Evidence from Environmental Measurements

The 58 compounds in Tables 2 and 3 (PBDEs and hexabromocyclododecane (HBCD) are common to both tables) represent a subset of chemicals predicted to be among the most persistent and bioaccumulative chemicals in current use. The 124 compounds listed by other screening programs (Table S1; 8 are found in Table 2 and 3) represent an additional subset of PB&T chemicals identified by slightly different criteria. Are there environmental measurements supporting these predictions? In Table 2 we estimate that only 2 of 30 compounds have been routinely measured, PBDEs (pentaBDE, no. 16; and HBCD, no. 22). PentaBDEs were identified in the 1980s in the United States and Europe (49) but were little studied until the late 1990s when it became apparent that they were increasing in concentration in humans and in environmental media. HBCD has been widely measured recently, especially in Europe (50). There is evidence Penta

BDE and HBCD are globally distributed based on measurements in biota in open oceans (50) and in the Arctic (51). Penta BDE is currently being considered for inclusion in the Stockholm Convention (52). Also on the list is perfluorooctanesulfonamidoethanol (PFOSE; no. 4) which has been widely detected in North American air (53). Perfluoroalkyl-sulfamido-alcohols have been shown to break down to perfluoroalkylsulfonates when reacted with OH-radical (5) and the global dispersion of PFOS is likely explained by the distribution of volatile precursors such as PFOSE. However, PFOSE is not listed in Table 3 because its estimated $AO\ t^{1/2}$ was 0.45 d in the Environment Canada categorization (34) although recent lab-based measurements give a value of 2 d (5). PFOSE is an example of the need to characterize the major degradation products of chemicals in commerce.

The cyclic siloxane in Table 2 (D6, no. 13) has recently been reported in a wide range of samples in Scandinavia along with D4 and D5, the cyclotetra- and cyclopentasiloxanes (54). The cyclic siloxanes are widely used additives in industrial products such as fuels, paints, and adhesives, and in consumer products such as cosmetics and shampoos (54). Relatively high concentrations were detected in air in urban locations ($0.02\text{--}4\text{ }\mu\text{g}/\text{m}^3$) and higher levels were observed in homes and sewage treatment plants. D4, D5, and D6 were also observed in fish and marine mammals (54). Although not yet confirmed by other studies, the results for siloxanes are consistent with the BCF, biodegradation, and $AO\ t^{1/2}$ predictions in Tables 2 and 3.

We estimate that there are environmental measurements for 8 of the 30 compounds in Table 3 (nos. 3, 4, 6, 14, 23, and 24, and closely related isomers/congeners, e.g., bromobiphenyl (no. 19) and chlorinated naphthalenes (no. 22)). It is very likely that others on the list could be analyzed by GC-MS because of their stability and semi-volatility indicated by high $AO\ t^{1/2}$ and $\log K_{aw}$ values, respectively.

Overall, about 12 of 58 could be said to be readily analyzed in environmental samples but fewer, perhaps 5, are part of regular monitoring programs. Similar conclusions can be reached when examining other screening projects (Table S1). Of the 132 chemicals identified potentially P&B or PB&T in Table S1 about 35 could be considered to be routinely determined in environmental samples while others (e.g., fluorinated alkanes, -alcohols, and sulfonamides) have had limited measurements and would be readily analyzable by GC-MS.

Chemical Analysis Methods for New Candidate P&B and LRAT Substances

As illustrated in Tables 2 and 3, and in other categorization projects discussed above, <20% of the categorized chemicals have been measured in environmental media. As programs such as REACH and HPVC initiatives proceed there is likely to be pressure to confirm risk and exposure assessment predictions with environmental measurements. However, this will require method development or at least refinements of existing procedures and sampling protocols, particularly if low level background concentration measurements are to be carried out to seek evidence for transport to remote regions. The monitoring of new P&B substances such as PBDEs and PFAs in environmental media has generally required detection at the low ng/g in biota or sediments, and pg/L in water, and thus has largely been driven by a few individual investigators with the resources to develop new separation techniques, synthesize analytical standards, and apply appropriate instrumentation for quantitative analysis. To commit time and resources, the lab (whether government, university, or industry/contract) must have a reasonable certainty of success and thus there is a tendency to look at the "low hanging fruit" first. For example, PBDEs could be

isolated and analyzed in the same fractions as those containing OCPs. Following along from PBDEs, there are increasing numbers of studies of other BFRs of similar bromine content such as HBCD (50, 55).

Another recent example is the detection of Dechlorane-Plus, a dodecachlorinated flame retardant which is a TSCA HPVC, in Great Lakes air, fish, and sediments (56). Dechlorane-Plus did not appear in the top 30 in Table 2 because QSPRs predict a low BCF (0.5) due to very high $\log K_{ow}$ (=11.3) and its low K_{aw} left it off of Table 3. This illustrates the potential for some false negatives although measurements in fish from Lake Erie suggest relatively low concentrations (0.14–0.9 ng/g lipid) compared to other current use organohalogen such as PBDEs. This “analog” approach for selection of chemicals has been successful, albeit for few chemicals currently in commerce, and has been done usually with limited knowledge of physical–chemical properties, or of the quantities in current or past use.

Developing appropriate multi-residue methodology is feasible for many P&B substances given that they are generally hydrophobic (high K_{ow}) and thus should be amenable to extraction, isolation, and separation systems currently used in determination of PCBs and legacy OCPs (57, 58), current use pesticides, and pharmaceuticals and personal care products (59). While preparation and extraction systems should be broadly applicable to a wide range of hydrophobics, refining the isolation steps to recover polar degradation products could be challenging because polarity of the molecules is important in chromatographic separations. For example, perfluoroalkylsulfonamides can also be isolated with these steps (60), however, the perfluoroalkyl acids (PFAs) typically require much more polar extraction conditions (61). Similarly metabolites such as halogenated phenolics must be separated from more nonpolar parent/precursor compounds by liquid–liquid partitioning or on solid-phase columns (62, 63).

Numerous analytical approaches are available for quantifying P&B chemicals. Semi-volatile, thermally stable, neutral compounds are usually amenable to separation by gas chromatography (GC). Fused silica open tubular capillary columns, generally coated with nonpolar or medium polarity chemically bonded liquid phases are almost universally used for GC separation of PCBs and OCPs (64, 65) and are applicable to many other organics. Given the resolution of capillary GC columns and high specificity of mass spectrometry (especially with high resolving power, i.e., milli mass resolution) this is the approach of choice for confirming the presence of P&B chemicals.

LC–tandem mass spectrometry has become widely used in the past 5 years for quantitative determination of many polar compounds, e.g., hormones and personal care products, CUPs, and transformation products of hydrophobic compounds such as OH-PCBs and PFAs (65, 66). LC–QTOF (quadrupole-time-of-flight mass spectrometry) and LC–TOF are also coming into wide use and the increased use of two-dimensional GC–TOF MS adds capacity for high resolving power to unambiguously identify chemicals of interest (67).

GC–MS or LC–MS can be applied qualitatively or semiquantitatively to identify chemicals without purified standards, e.g., with technical or commercial products containing the substance of interest, or by searching mass spectral databases for exact matches. However, routine quantitative analysis requires analytical standards of known purity, preferably certified by analysis using multiple laboratories and/or methodologies. Furthermore, it is usually necessary to have specific congeners or isomers available to properly quantify the chemicals and stable isotope-labeled (^{13}C , ^{18}O , or ^2H) standards for quantitative work. The acquisition of suitable standards is thus another major challenge for any multichemical screening of P&B substances.

Challenges for Environmental Chemists

This overview of ongoing screening and categorization of existing chemicals indicates that there are widely used substances that are predicted to meet screening criteria as P&B and LRAT chemicals but that are not currently analyzed in environmental matrices. The number of compounds may be small in relation to total chemicals in commerce. For example, the Canadian categorization has identified about 5.5% of 11,317 substances as meeting P&B criteria (34) and as noted above, sorting by LRAT characteristics reduces this number by a factor of 10. Other surveys have suggested the fraction of industrial chemicals meeting all three PB&T criteria is 1–2% (23, 68). Not assessed here are new substances whose molecular structures are considered confidential business information such as some replacements for PBDEs. The lists developed here, and by other investigators (23, 37, 68), are potentially a very good source of chemicals for addressing the issue of previously unrecognized POPs. However, up to now there is little evidence that environmental chemists have directed their measurements for new chemicals based on this screening and categorization activity. Models are available to guide monitoring efforts, e.g., RAIDAR (69) is a model that gets around lack of emissions data by estimating environmental fate and transport, bioaccumulation, and exposure using a unit emission rate (69). The predicted physical–chemical properties such as $\log K_{ow}$, $\log K_{aw}$, and $\text{AO } t_{1/2}$ are useful for determining the “analyzability” of candidate chemicals. But environmental analytical chemists need guidance on what matrices to look at. Production volume and use information is essential for helping to set priorities. Particularly crucial are data on emissions from end use, e.g., from industrial processes and consumer products, so that more sophisticated environmental fate models can be applied (8). Also needed is more information on UVCBs which, due to their complexity, are difficult to screen and to analyze. To fully address the issue we need to be able to identify persistent transformation products, and innovative, new, analytical methods may be needed to detect them along with parent compounds. It is time that the modeling and environmental measurement community got together to examine this issue in detail.

Acknowledgments

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Supporting Information Available

More detailed information on the categorization of the Canadian Domestic Substances list; Table S1 list of 124 chemicals identified in recent screening and categorization studies. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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